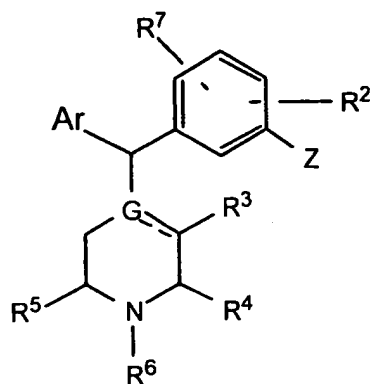


## ABSTRACT OF THE DISCLOSURE

A method of reducing, treating or preventing drug-mediated respiratory depression, muscle rigidity, or nausea/vomiting in an animal, incident to the administration to said animal of a mixed delta/mu opioid agonist or a respiratory depression-mediating drug, comprising administering to the animal receiving said drug an effective amount of a delta receptor agonist compound. The delta agonist compound may comprise a compound of the formula:



(I)

wherein:

Ar is a 5- or 6-member carbocyclic or heterocyclic aromatic ring with atoms selected from the group consisting of carbon, nitrogen, oxygen and sulfur, and having on a first carbon atom thereof a substituent Y and on a second ring carbon thereof a substituent R<sup>1</sup>,

Y is selected from the group consisting of:

hydrogen;

halogen;

C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl;

C<sub>1</sub>-C<sub>6</sub> haloalkyl;

C<sub>1</sub>-C<sub>6</sub> alkoxy;

C<sub>3</sub>-C<sub>6</sub> cycloalkoxy;

sulfides of the formula  $SR^8$  where  $R^8$  is  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $C_3$ - $C_6$  cycloalkyl, arylalkyl having a  $C_5$ - $C_{10}$  aryl moiety and an  $C_1$ - $C_6$  alkyl moiety, or  $C_5$ - $C_{10}$  aryl;

sulfoxides of the formula  $SOR^8$  where  $R^8$  is the same as above;

5 sulfones of the formula  $SO_2R^8$  where  $R^8$  is the same as above;

nitrile;

$C_1$ - $C_6$  acyl;

alkoxycarbonylamino (carbamoyl) of the formula  $NHCO_2R^8$  where  $R^8$  is the same as above;

10 carboxylic acid, or an ester, amide, or salt thereof;

aminomethyl of the formula  $CH_2NR^9R^{10}$  where  $R^9$  and  $R^{10}$  may be the same or different, and may be hydrogen,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $C_2$ - $C_6$  hydroxyalkyl,  $C_2$ - $C_6$  methoxyalkyl,  $C_3$ - $C_6$  cycloalkyl, or  $C_5$ - $C_{10}$  aryl, or  $R^9$  and  $R^{10}$  together may form a ring of 5 or 6 atoms, the ring atoms selected from the group consisting of N and C;

15 carboxamides of the formula  $CONR^9R^{10}$  where  $R^9$  and  $R^{10}$  are the same as above, or  $C_2$ - $C_{30}$  peptide conjugates thereof; and

sulfonamides of the formula  $SO_2NR^9R^{10}$  where  $R^9$  and  $R^{10}$  are the same as above;

Z is selected from the group consisting of:

20 hydroxyl, and esters thereof;

hydroxymethyl, and esters thereof; and

amino, and carboxamides and sulfonamides thereof;

G is carbon or nitrogen;

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$R^1$  is hydrogen, halogen, or  $C_1$ - $C_4$  alkyl,  $C_2$ - $C_4$  alkenyl,  $C_1$ - $C_4$  alkynyl;

$R^2$  is hydrogen, halogen, or  $C_1$ - $C_4$  alkyl,  $C_2$ - $C_4$  alkenyl,  $C_1$ - $C_4$  alkynyl;

$R^3$ ,  $R^4$  and  $R^5$  may be the same or different, and are independently selected from hydrogen and methyl, and wherein at least one of  $R^3$ ,  $R^4$  or  $R^5$  is not hydrogen, subject to the proviso that the total number of methyl groups does not exceed two, or any two of  $R^3$ ,  $R^4$  and  $R^5$  together may form a bridge of 1 to 3 carbon atoms;

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$R^6$  is selected from the group consisting of:

hydrogen;

$C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl;

$C_3$ - $C_6$  cycloalkyl;

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arylalkyl having  $C_5$ - $C_{10}$  aryl and  $C_1$ - $C_6$  alkyl moieties;

alkoxyalkyl having  $C_1$ - $C_4$  alkoxy and  $C_1$ - $C_4$  alkyl moieties;

$C_2$ - $C_4$  cyanoalkyl;

$C_2$ - $C_4$  hydroxyalkyl;

aminocarbonylalkyl having a  $C_1$ - $C_4$  alkyl moiety; and

$R^{12}COR^{13}$ , where  $R^{12}$  is  $C_1$ - $C_4$  alkylene, and  $R^{13}$  is  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

and

$R^7$  is hydrogen or fluorine,

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or a pharmaceutically acceptable ester or salt thereof.